Center for Drug Evaluation and Research

WHAT'S NEW IN REGULATORY SCIENCE

Fall/Winter 2020

Brought to you by the Office of Translational Sciences (OTS) in collaboration with the Office of Communications (OCOMM) within the Center for Drug Evaluation and Research (CDER)

What's New in Regulatory Science is a quarterly newsletter from the Food and Drug Administration's (FDA's) Center for Drug Evaluation and Research (CDER). It features new developments, opportunities, and initiatives in regulatory science, with the goal of advancing medical product development.

Please share this message and the sign-up link with colleagues. If you have comments or questions, please contact us at OTSCommunications@fda.hhs.gov.

COVID-19 (CORONAVIRUS DISEASE 2019 PANDEMIC) FDA NEWS RELEASES

- **FDA Approves First Treatment for COVID-19**

  On October 22, 2020, the U.S. Food and Drug Administration approved the antiviral drug Veklury (remdesivir) for use in adult and pediatric patients 12 years of age and older and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. Learn more.

- **FDA Authorizes Monoclonal Antibody for Treatment of COVID-19**

  On November 10, 2020, the U.S. Food and Drug Administration issued an emergency use authorization (EUA) for the investigational monoclonal antibody therapy bamlanivimab for the treatment of mild-to-moderate COVID-19 in adult and certain pediatric patients. Specifically, bamlanivimab is authorized for patients with positive results of direct SARS-CoV-2 viral testing

who are 12 years of age and older weighing at least 40 kilograms (about 88 pounds), and who are at high risk for progressing to severe COVID-19 and/or hospitalization. High risk patients include those who are 65 years of age or older, or who have certain chronic medical conditions. The data supporting this EUA for bamlanivimab are based on an interim analysis from a phase two randomized, double-blind, placebo-controlled clinical trial in 465 non-hospitalized adults with mild to moderate COVID-19 symptoms. The treatment was shown to reduce the viral load, COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo. The safety -and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated. Bamlanivimab is not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy.

- **FDA Authorizes Drug Combination (Baricitnib and Remdesivir) for Treatment of COVID-19**

  On November 19, 2020, the U.S. Food and Drug Administration issued an emergency use authorization (EUA) for the drug baricitinib, in combination with remdesivir, for the treatment of suspected or laboratory confirmed COVID-19 in hospitalized adults and pediatric patients two years of age or older requiring supplemental oxygen, invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

  In a clinical trial of hospitalized patients with COVID-19, baricitinib, in combination with remdesivir, was shown to reduce time to recovery within 29 days after initiating treatment compared to patients who received a placebo with remdesivir. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated. Baricitinib is not authorized or approved as a stand-alone treatment for COVID-19.

- **FDA Authorizes Drug Combination (casirivimab and imdevimab) for Treatment of COVID-19**

  On November 21, 2020, the FDA issued an EUA for casirivimab and imdevimab, administered together by intravenous (IV) infusion, for the treatment of mild to moderate COVID-19 in adults and pediatric patients (12 years of age or older weighing at least 40 kilograms [about 88 pounds]) with positive results of direct SARS-CoV-2 viral testing and who are at high risk for progressing to severe COVID-19. In a clinical trial of patients with COVID-19, casirivimab and imdevimab, administered together, were shown to reduce COVID-19-related hospitalization or emergency room visits in patients at high risk for disease progression within 28 days after treatment when compared to placebo. The safety and effectiveness of this investigational therapy for use in the treatment of COVID-19 continues to be evaluated. Casirivimab and imdevimab are not authorized for patients who are hospitalized due to COVID-19 or require oxygen therapy.

COVID-19 UPDATES (From September 19, 2020 to December 20, 2020)

The FDA is engaged in numerous activities to protect and promote public health during the COVID-19 pandemic. For CDER, these efforts include accelerating development of treatments for COVID-19, maintaining and securing drug supply chains, providing guidance to stakeholders, advising developers on how to handle clinical trial issues, and keeping the public informed. Information on some of CDER's efforts related specifically to drugs and COVID-19 can be found in the summer issue of the newsletter. Click here for details. Newer updates are provided below:

Coronavirus (COVID-19) Drugs Web Page

https://www.fda.gov/drugs/emergency-preparedness-drugs/coronavirus-covid-19-drugs

FDA COVID-19 Initiatives

- FDA COVID-19 Response At-A-Glance Summary as of November 20, 2020
  https://www.fda.gov/media/137005/download

- Coronavirus Treatment Acceleration Program (CTAP)
  FDA has created a special emergency program for possible COVID-19 therapies, the Coronavirus Treatment Acceleration Program (CTAP). As of November 10, 2020, the FDA updated the dashboard on the CTAP webpage. As of October 31, more than 560 drug development programs were in planning stages, over 370 trials had been reviewed by FDA, 5 COVID-19 treatments were currently authorized for emergency use, and 1 treatment was approved by FDA for use in COVID-19. Click here for details.

- Developing and Manufacturing Drugs Including Biological Products
  The FDA consolidated existing resources for stakeholders to easily access information about drug and biological product development and manufacturing, including for products to diagnose, cure, mitigate, treat or prevent COVID-19 and for other critically needed products to treat symptoms of COVID-19 or to provide supportive care to those with COVID-19. Click here for details.

- Updates on the guidance, "Conduct of Clinical Trials of Medical Products during COVID-19 Public Health Emergency"

  The FDA continues to add content to the question-and-answer appendix in its guidance titled "Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency." FDA issued this guidance because the agency recognizes that the public health

emergency may impact the conduct of clinical trials of medical products, including drugs, devices, and biologics. Challenges in conducting clinical trials may arise from isolation practices, site closures, travel limitations, interruptions to the supply chain for the investigational product, or other considerations if site personnel or clinical trial participants contract COVID-19.

- FDA Updates on hand sanitizers
  FDA continues to monitor hand sanitizer products for possible methanol or 1-propanol contamination, as well as subpotency where certain hand sanitizer products have concerningly low levels of ethyl alcohol or isopropyl alcohol. FDA continues to update its do-not-use list of hand sanitizers at www.fda.gov/unsafehandsanitizers. FDA also continues to update the hand sanitizer guidances, as needed.

- COVID-19 Educational Resources
  FDA has assembled health education materials, educational videos, podcasts, social media tool kits, consumer articles, and other resources to help inform various stakeholders about the COVID-19 pandemic.

FDA HIGHLIGHTS

Pharmaceutical Users Software Exchange (PhUSE)/FDA Data Science Innovation Fridays Webinar Series

Pharmaceutical Users Software Exchange (PhUSE) is an expanding, global society with a global membership of clinical data scientists. The Pharmaceutical Users Software Exchange (PhUSE) Computational Science Collaborations provides a platform for academia, regulators, industry, and technology providers to address computational science needs in support of regulatory review. This collaboration is supported by PhUSE, CDER, and the Center for Biologics Evaluation and Research (CBER), resulting in the development of resources that improve preparation and analysis of regulatory data and associated documentation. Webinars are held every Friday, at 9:00 a.m. (EDT). To view the schedule, go to: PHUSE/FDA Data Science Innovation Challenge

Regulatory Science Extramural Research and Development Projects

To spur innovation in the field of regulatory science, FDA funds extramural research using various contract mechanisms and grants to address broad Agency challenges within FDA's scientific priority areas. Since 2012, FDA has been soliciting proposals to advance the state of the art within these areas through a specialized contract mechanism known as FDA's Broad Agency Announcement (BAA). Click here for details.

Centers of Excellence in Regulatory Science and Innovation (CERSIs)

FDA's Centers of Excellence in Regulatory Science and Innovation (CERSIs) are collaborations between FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges. Evolving areas of science are promising new approaches to improving our health while demanding new ways to evaluate the safety and effectiveness of the products FDA regulates. Click here for details.

List of online educational resources and trainings from FDA

A list of online educational resources and trainings at FDA, have been added to the University of Rochester's Clinical & Translational Science Institute resources website, as part of the CTSA (Clinical and Translational Science Awards)/NCATS (National Center for Advancing Translational Science) effort.

Meet the Faces Behind FDA Science

Every day, FDA scientists carry out scientific research and regulatory actions that have a profound impact on the health and well-being of all Americans. They use their expertise to promote public health and foster therapeutic innovations. The FDA scientists highlighted in this section talk about their passion for the work they do, the Agency's pioneering regulatory science culture and opportunities for professional growth, and why they love working at FDA. Click here to read more

CDER Highlights

CDER Conversations

https://www.fda.gov/drugs/news-events-human-drugs/more-cder-conversations

RECENT CDER IMPACT STORIES

CDER is continuing to highlight its regulatory science research in a series of regulatory science impact stories. Recent posts include:

A consistent benefit of adding a CDK 4/6 inhibitor to a hormonal agent in important subgroups of patients with hormone receptor–positive, HER2-negative advanced or metastatic breast cancer

When CDER researchers analyzed several important subgroups of patients treated with modern hormone-based regimens, they found that the

benefit of adding a CDK 4/6 inhibitor to a hormonal agent was consistent across all subgroups. This study provides important data to clinicians and patients for making treatment decisions and will inform future trials of therapies for hormone receptor–positive, HER2-negative metastatic breast cancer. Learn more.

Improving Schizophrenia Trials

Based on their analyses of schizophrenia drug trials submitted by drug developers, CDER researchers have identified ways in which these trials could be streamlined while not compromising their sensitivity. Their findings are outlined in a recent issue of JAMA Psychiatry. Learn more.

Factors that May Predict the Likelihood of Generic Drug Marketing Applications

CDER researchers recently analyzed how drug characteristics, regulatory actions, and economic factors influence whether generic drugs become available for a brand-name drug. A major finding was that for complex drugs (for example those with complicated structures, compositions, or modes of delivery) submissions of applications for generics was less likely. However, for complex drugs that were not new molecular entities, the presence of an FDA product-specific guidance increased the likelihood of an ANDA submission for a generic. Learn more.

Public Posting of a Comprehensive Surrogate Endpoint Table for CDER- and CBER-Regulated Products

Surrogate endpoints are biomarkers that are reasonably likely to predict a clinical benefit but are not themselves a measure of clinical benefit. Common examples include blood pressure, hemoglobin A1c, and HIV viral load. CDER has assembled and published a carefully annotated table of such endpoints that allows stakeholders to determine which of them might reasonably be used for marketing applications, thereby enabling transparency and expediting future drug development. Learn more.

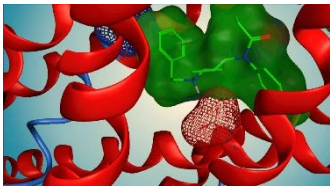
RECENT SPOTLIGHT ON CDER SCIENCE

CDER continues with its *Spotlight on CDER Science* series featuring the Center's noteworthy scientific and research-oriented activities. Recent *posts* include:

New methods to detect nitrosamine contaminants in drug products

Since 2018, multiple drug products have been recalled due to the presence of unacceptable amounts of nitrosamines. To help test drug products for these carcinogenic chemicals, CDER scientists have developed and publicly shared multiple methods, including gas chromatography-mass spectrometry and liquid chromatography-MS (LC-MS), for detecting and quantifying these substances in drug products, even when present in amounts well below the FDA acceptable intake levels. Learn more.

Developing best practices for modeling and simulation



Most new drug applications now contain evidence from modeling and simulation, and therefore it is important to identify best practices and evaluate the reliability of the models. With colleagues in CDRH and CBER, CDER investigators evaluated the applicability of an evidentiary framework known as the V&V40 standard to physiologically based pharmacokinetic models and report that aspects of the standard could be relevant to this class of models and potentially expanded to other modeling approaches. Learn more.

Affirming the effectiveness of generics for a widely used drug to treat hypothyroidism

To address concerns in the medical community that generic forms of levothyroxine may not be as effective as the brand name versions of the drug, CDER researchers have conducted a retrospective analysis of clinical outcomes using insurance claims data. The real-world evidence provided from this study should reassure clinicians and patients that despite its narrow therapeutic index, generic levothyroxine is as effective as the brand-name drug as initial therapy for hypothyroidism. Learn more.

IN PRESS

In Press

"Unless otherwise indicated, the opinions expressed in these articles are those of the authors and should not be interpreted as the position of the U.S. Food and Drug Administration."

Recent Scientific Publications by FDA/CDER Staff can be found here

Some examples are provided below:

Immunomodulatory Therapeutic Proteins in COVID-19: Current Clinical Development and Clinical Pharmacology Considerations.

Ji P., Chen […] Sahajwalla, C G, *J Clinical Pharmacol no. 10* 2020 *60*, 1275-1293.

In this review, several CDER authors summarize the clinical pharmacology considerations in the development of immunomodulatory therapeutic proteins for mitigating the heightened inflammatory response identified in COVID-19.

The dynamic changes in cytokine responses in COVID-19: a snapshot of the current state of knowledge.

Buszko M, Park JH […] Rosenberg AS, Nat Immunol 2020 Oct;21(10):1146-51.

NIH and FDA authors provide a summary of an online conference organized by the NIH/FDA Immunology and Cytokine Interest Groups to discuss our rapidly changing understanding of COVID-19-related cytokine responses in different stages of infection, including the etiology of COVID-19, downstream consequences and possible mitigation strategies.

UPCOMING EVENTS

Information on upcoming meetings, conferences, and workshops sponsored or co-sponsored by CDER and be found is available on FDA webpages. For details on each event, click here.

CAREER OPPORTUNITIES

FDA continues to recruit and retain a world-class workforce dedicated to protecting and promoting the public health. Information on job vacancies, employment events, and hiring programs can be found by following @FDAJobs on Twitter and by visiting FDA's LinkedIn page and the Jobs at CDER and the Career Opportunities at CDER webpages. In addition, you can contact OTS directly at CDEROTSHires@fda.hhs.gov. Help us spread the news through your social media networks!

For more information, please visit the FDA In Brief webpage.

Scientific Internships and Fellowships / Trainees and Non-U.S. Citizens

Whether you're an undergraduate looking to pursue a career in science, a graduate student seeking experience in regulatory science, a postgraduate looking for fellowship opportunities, or a senior scientist pursuing research experience in your field of expertise, FDA offers you many paths to learning about the exciting field of regulatory science. Click here for more information.